2023 Draft Annual Report - On going work

In this guide

This is a paper for discussion.

This does not represent the views of the Committee and should not be cited.

Existing health-based guidance values (HBGVs) for T2 & HT2 mycotoxins

1.89 T2 and HT2 are mycotoxins which are produced by Fusarium fungi and found in cereal grains and their products. The COT last assessed T2 and HT2 mycotoxins in 2018 when reviewing the diet of infants aged 0 to 12 months and young children aged 1 to 5 years. At the time, the COT agreed with the group Acute Reference Dose (ARfD) and group Tolerable Daily Intake (TDI) for T2 and HT2 established by the European Food Safety Authority (EFSA) in 2017.

1.90 Commission Recommendation 2013/165/EU sets out indicative levels for T2/HT2 in a number of food commodities. However, the European Commission has now proposed replacing these current indicative values with legislative limits for T2/HT2 in the EU. These draft legislative limits are much lower that the pre-existing indicative values and may have an impact on UK industry, especially on cereals. Currently there is no retained EU law covering T2 and/or HT2. However, the FSA has had extensive dialogue with industry, and has previously been involved in EU working groups on the development of appropriate maximum levels.

1.91 The COT were asked to consider the existing HBGVs for T2/ HT2 published by EFSA and by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), and to confirm an appropriate HBGV for FSA risk assessments. The Committee reviewed the available data on the absorption, distribution, metabolism, and excretion of T2 and HT2 in animals and humans, as well as their toxic effects, such as haematotoxicity, immunotoxicity, emesis, and reduced body weight used in the establishment of the HBGVs along with the mode of action, species sensitivity, and dose-response relationships of T2 and HT2.

1.92 The Committee noted that it was unclear why JECFA did not include an uncertainty factor to account for interspecies differences; this could be because JECFA had considered emesis to be a direct effect rather than a central effect, and therefore no variability would be expected in the kinetics. The COT did not necessarily disagree, but clarification on this would be helpful when the full toxicological monograph was available.

1.93 Overall, the Committee was content with the use of EFSA's HBGVs for future risk assessments.

1.94 The FSA intends to assess the level of risk arising from dietary exposure to T2/HT2 for UK consumers through a call for UK occurrence data, once completed, this will be presented to the Committee for their consideration.

Position paper on chitosan in bio-based food contact materials

1.95 As part of an ongoing programme of work on bio-based food contact materials (BBFCMs), the Committee discussed the potential allergenicity and environmental impacts of chitosan, a biodegradable polysaccharide derived from chitin.

1.96 Chitin is mainly obtained from crustacean shells but can also be derived from fungi and insects. Chitosan is produced by deacetylating chitin. Both chitin and chitosan have applications in food, medicine, and biotechnology. BBFCMs containing chitin or chitosan are used in applications such as films, coatings, and drinking straws.

1.97 The Committee considered information on the prevalence, causes, and symptoms of shellfish allergy, which is mainly triggered by tropomyosin, a muscle protein found in crustaceans and molluscs. The possibility of cross-reactivity between shellfish and other sources of chitin or chitosan, such as insects and fungi was also considered.

1.98 The Committee further considered the challenges and uncertainties regarding the migration, degradation, and allergenicity of these materials.

1.99 A position paper setting out the views of the Committee will be published in 2024.

Hepatotoxicity of green tea catechins

1.100 In 2017, following a series of reports of adverse effects on the liver following the consumption of green tea supplements, the European Commission requested the European Food Safety Authority (EFSA) to assess the available information on the safety of green tea catechins (principally - epigallocatechin-3-gallate (EGCG)) from all dietary sources including preparations such as food supplements and traditional infusions, with a focus on liver toxicity. At that time, and at the request of the Department of Health and Social Care (DHSC), who have the policy lead for food supplements in England, the FSA Chemical Risk Assessment Unit team reviewed the EFSA opinion informally and agreed with its conclusions.

1.101 Following a request to the Food Standards Agency from the Nutrition Labelling Composition and Standards (NLCS) Common Framework on behalf of the UK, the COT have been asked to evaluate whether the conclusions of the 2018 EFSA opinion are still applicable (EFSA, 2018), in view of any new data that have become available since its adoption, to enable them to consider the next steps.

1.102 The 2018 EFSA opinion itself and its evaluation by the COT, focus on green tea catechins and the associated cases of probably idiosyncratic hepatotoxicity, rather than being a safety assessment of either green tea catechins or green tea infusions and extracts more generally.

1.103 A discussion paper was presented to the Committee in September 2021, since which drafts of the statement have been reviewed, with the final substantive discussion being held in May 2023.

1.104 The statement will be finalised by the COT in 2024.

Review of titanium dioxide as a food additive

1.105 Following the publication of the European Food Safety Authority (EFSA) opinion on titanium dioxide in 2021, which concluded that titanium dioxide could no longer be considered ‘safe’ for use in food, the Food Standards Agency (FSA) initiated a review of the EFSA opinion. The EFSA opinion was presented to the COM in June 2021 (MUT/2021/03) and to the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) in July 2021 (TOX/2021/36). The COM had several concerns over the EFSA opinion on the genotoxicity of titanium dioxide. Due to this and following the advice of the COT the FSA initiated an independent evaluation of the safety of the use of titanium dioxide as a food additive.

1.106 In October 2021, paper MUT/2021/08 was presented to the COM, which summarised the available genotoxicity on titanium dioxide. Members considered that it was not possible to evaluate the genotoxicity of titanium dioxide at that stage. The COM suggested a sifting approach to the available genotoxicity should be adopted as a first step before evaluation. The Chair of the COM, a subgroup of the COM and the secretariat subsequently attended meetings to discuss and agree the criteria and methodology for sifting to identify suitable papers for the evaluation of titanium dioxide.

1.107 At the COM June 2022 meeting, paper MUT/2022/05 provided information and papers on approaches relating to the sifting and evaluation of the quality genotoxicity studies and evaluating data on nanomaterials. As an update since that meeting, members were informed that a sub-group of the COM had met to discuss the process to select relevant and appropriate studies to be reviewed by the committee. A proforma had been produced, which would be shared with members. This considered two levels, namely, whether the characteristics of the test material had been sufficiently described (e.g., micro or nano sized particles) and the quality and reliability of how the genotoxicity studies had been conducted.

1.108 In March, July, September and October 2023, papers TOX/2023/16, TOX/2023/32, TOX/2023/44 and TOX/2023/56 were presented to the COT,

respectively. These papers summarised the following topics and endpoints: Absorption, Distribution, Metabolism, Excretion (ADME), Aberrant Crypt Foci, Reproductive and Developmental Toxicity, immunotoxicity, neurotoxicity and the derivation of a potential Health-Based Guidance Value for titanium dioxide, dependent on the outcome of the review by the COM.

1.109 In the October 2023 meeting, COT members were kept updated with the progress of the COM sub-group review. It was noted that a third draft statement along with the concluding statement on the genotoxic potential of titanium dioxide would be finalised by May 2024. The COM sub-group would be considering potential mechanisms and whether the effects were linked to the nanoparticle fraction.

Lead in the maternal diet

1.110 The Scientific Advisory Committee on Nutrition (SACN) is reviewing the scientific evidence that bears on the Government's dietary recommendations for women of childbearing age. The SACN have requested that the Committee on Toxicity (COT) review the risks of toxicity from chemicals in the maternal diet, including lead.

1.111 Lead is a heavy metal which is ubiquitous in the environment and is thus present in the diet of the general population, including women of childbearing age. However, dietary lead levels have fallen since the phasing out of lead in petrol, plumbing and paints.

1.112 Chronic lead poisoning from low level, repeated exposure gives clinical signs of persistent vomiting, encephalopathy, lethargy, delirium, convulsions, and coma. The central nervous system, erythropoietic system and the kidneys are most affected by lead exposure, but all bodily systems can be adversely affected. In pregnant women, lead can cause increased blood pressure and may be associated with preeclampsia and premature birth.

1.113 Potential risks from maternal exposures to lead were characterised by margins of exposure (MOEs), calculated as the ratio of the benchmark dose level (BMDL) to estimated exposures from diet, soil and air. A BMDL01 has been set for the reduced development of intellectual function in offspring. Specifically, a dietary exposure of 0.5 µg/kg bw/day was associated with a 1% change in full scale IQ score (EFSA 2010). As the BMDL was for a small effect, derived from pooled analysis of multiple cohort studies of exposures in infants and children, it is likely to be conservative and protective for all other adverse effects of lead in

all populations. EFSA therefore concluded that a margin of exposure of 10 or greater should be sufficient to ensure that there was no appreciable risk of a clinically significant effect on IQ. At lower MOEs, but greater than 1.0, the risk is likely to be low, but not such that it could be dismissed as of no potential concern (EFSA, 2010).

1.114 In 2013, the COT added that an MOE of >1 can be taken to imply that at most, any risk is likely to be small. MOEs <1 do not necessarily indicate a concern, but scientific uncertainties mean that a material risk cannot be ruled out. This applies particularly when MOEs are substantially <1. The COT further concluded, in agreement with EFSA, determined that neurodevelopmental effects represent the most sensitive endpoint for effects in the developing foetus whilst also being protective of the other toxicological end points in the mother (COT, 2013).

1.115 The Committee assessed exposure to lead from various sources (food, drink, air, soil and dust). Overall, the committee concluded that lead toxicity will depend on total exposure from all sources, it therefore considered an aggregate exposure to determine an overall likely level of risk.

1.116 A combined exposure assessment, considering exposure to lead from all sources, relative to the BMDL01 of 0.5 µg/kg bw/day, gives an MOE range of 1-2 depending on the individual contribution to the total of each source (food, drinking water, soil/dust). A scenario in which there are high levels of exposure to lead from food, drinking water and soil/ dust would result in an MOE of 1, however, this assumes a worst-case for all sources for a prolonged period of time. In a scenario where there are average levels of exposure to each source, the MOE is 2. These MOE values indicate that an aggregate risk of toxicity from lead in relation to the maternal diet and other potential sources of maternal exposure is likely to be small.

1.117 A statement setting out the Committee’s assessment of lead will be published in 2024.

Arsenic in the maternal diet

1.118 As part of the work on the maternal diet, the COT was asked to consider the potential effects of excess arsenic (As) intake. The COT most recently reviewed arsenic in 2016 as part of the programme of work with SACN on the diets of infants and young children and provided comments on the most recent Draft EFSA opinion (2023) for public consultation.

1.119 Arsenic is a metalloid that occurs in the environment in a variety of forms as a result of both natural and anthropogenic activity. Acute exposure to inorganic arsenic (iAs) results in clinical symptoms such as nausea, vomiting, colicky abdominal pain, and diarrhoea. Chronic iAs exposure results in non-specific symptoms including abdominal pain, diarrhoea, and sore throat and can result in multisystem disease and malignancy, including cancer, skin lesions, developmental effects, cardiovascular disease, neurotoxicity and diabetes. Health outcomes resulting from iAs toxicity varies between individuals and different geographical areas.

1.120 It is generally accepted that iAs compounds are more toxic than the organic As compounds that are commonly found in fish, seafood, and other marine organisms (arsenobetaine, arsenosugars, and arsenolipids).

1.121 The potential risks from maternal exposures to inorganic arsenic were characterised by margins of exposure (MOEs), calculated as the ratio of the benchmark dose level (BMDL) to estimated exposures from diet, soil and air (individually and aggregated). Previously in 2016, the COT concluded that the JECFA (2011) BMDL0.5 of 3.0 µg/kg bw/day for lung cancer should be used in the characterisation of the potential risks from exposure to inorganic arsenic. The JECFA BMDL was based on exposure to iAs via drinking water from shallow wells. The majority of the epidemiological studies have focused on exposures to iAs via drinking water and have not measured or reported total dietary exposure to iAs. The COT also previously concluded that an MOE of 10 or above would be considered of a low concern.

1.122 The main contribution to As exposure in the UK is from dietary sources; non-dietary sources such as water, air, soil, and dust contributed negligible quantities.

1.123 The aggregate exposure for iAs from all sources for average consumers resulted in an MOE of 11, while the MOE for high consumers was 6. A risk to the health of women of childbearing age, specifically for high consumers, could not be excluded.

1.124 During the COT’s evaluation of arsenic in the maternal diet EFSA published their draft opinion on arsenic in food. The Committee agreed that they would wait until EFSA formally publish their opinion, expected in early 2024, to finalise their discussions and subsequent COT statement, later in 2024.

Discussion paper on the effects of pica during pregnancy

1.125. As part of the discussions regarding the contribution of soil and dust to lead exposure in the maternal diet, the Committee requested further information on the practice of pica, the consumption of non-food substances, in pregnant women.

1.126 Members noted that the main concern with respect to pica was geophagia (the consumption of earth, soil, or clay), primarily of soil of ancestral origin, due to the presence of contaminants, notably heavy metals. Geophagia (and pica more generally), was not a practice uniformly distributed across the population and the cultural differences in consumption of soil would mean that there could be large differences in exposure. Furthermore, exposure would be difficult to determine, as the background levels of heavy metals in UK soils would not be appropriate to estimate exposure, as the soils consumed as part of geophagia are often imported from around the world.

1.127 The Committee concluded that the risks of pica behaviour could not be quantified, however, Members considered whether or not pica behaviour should be discouraged on health grounds. Although anecdotally, anaemia had been associated with pica, the relevance of this was difficult to interpret as anaemia was almost ubiquitous in pregnancy and that it may be necessary to stratify by socioeconomic status before being able to understand the nature and the direction of the relationship between pica and anaemia.

1.128 The Committee agreed that the chemicals of concern from pica were predominantly heavy metals as these had largely been covered elsewhere in the review of the maternal diet. Therefore, it was concluded that, given the limited data set, it would be more appropriate to include a general consideration of pica in the overarching statement for the maternal diet, which would be published at the completion of this work.

Ginger in the maternal diet

1. 129 As part of the current programme of work on the maternal diet, the Committee considered the use of herbal dietary supplements during pregnancy. These were supplements that were not officially recommended by the relevant authorities, but which were promoted by anecdotal evidence and unofficial sources as having various purported benefits. Ginger was identified as one of the supplements that should be considered in more detail.

1.130 Ginger (Zingiber officinale) is a flowering tropical plant originating in Southeast Asia and grown in warm climates including China, India, Africa and the

Caribbean. The rhizome (underground stem) of the ginger plant is commonly used as a spice and flavouring in many countries around the world and is increasingly growing in popularity as a natural remedy due to its purported immune system-boosting properties and also for motion sickness and post-operative nausea and vomiting.

1.131 The COT have previously reviewed the potential effects of ginger and in particular, the use of ginger supplements during pregnancy and lactation, reviewing the available data on toxicity to the mother, effects on the development of the fetus or embryo, and possible interactions with medicines. A revised statement was reviewed by the Committee in 2023 and included additional studies which had previously been identified by the COT to further inform the database on the possible influence of ginger components on cyclooxygenase (COX) and prostaglandin activity.

1.132 A further draft of the statement will be brought back to the Committee in 2024 with a clearer distinction between the forms of ginger; in particular, those used as traditional culinary spice compared to the more concentrated forms of ginger such as ‘shots’. Further clarification on several points highlighted by the COT would also be provided.

1.133 The statement will be finalised by the COT in 2024.

The potential risks from ergot alkaloids in the maternal diet

1.134 As part of the ongoing programme of work on the maternal diet, the Committee were asked whether exposure to ergot alkaloids (EAs) would pose a risk to maternal health.

1.135 Ergot alkaloids (EA) are secondary metabolites produced by the fungi families Clavicipitaceae and Trichocomaceae, with Claviceps purpurea being the most widespread Claviceps species in Europe. Based on their occurrence and the available toxicological data the European Food Safety Authority (EFSA) considered six EAs in their risk assessment in 2005, namely: ergotamine, ergocornine, α-ergocryptine, ergosine, ergocristine (peptide ergot alkaloids) and ergometrine (a lysergic acid amide). EFSA further included both forms (-ine and inine) in their assessment, while the -inine forms are considered biologically inactive interconversion occurs under various conditions (EFSA, 2005, Tasker and Wipf, 2021). Bromocriptine is synthetic ergoline derivate and it is used in the treatment of Parkinson’s disease and pituitary tumours (Herdman et all., 2001).

1.136 Due to their structural similarities to neurotransmitters, EAs can act as agonists or antagonists of noradrenaline, dopamine and serotonin neurotransmitters (Arroyo-Manzanares et al., 2017, Fitzgerald and Dinan, 2008) and have been reported to produce direct peripheral effects such as uterotonic action or vasoconstriction, indirect peripheral effects such as serotonin antagonism or adrenergic blockade, and central nervous system (CNS) effects such as induction of hypothermia and emesis (EFSA, 2012).

1.137 The potential risk from EAs in the maternal diet was discussed by the Committee in 2022. It was concluded that EAs would not have adverse effects on maternal health at likely levels of exposure. A statement on ergot alkaloids will be published in 2024.

Statement on the risk assessment of cow’s milk in children aged 1 to 5 years, in the context of plant-based drinks evaluations

1.138 The Department for Health and Social Care’s (DHSC) is conducting an Equalities Analysis covering both the Nursery Milk Scheme and the Healthy Start Scheme, which considers equalities issues posed by the current legislation as it pertains both to plant-based drinks, and also to animal milks other than cow’s milk. DHSC is keen to ensure that this Equalities Analysis reflects the most up-to-date advice on safety and toxicity issues from COT, and on nutritional issues from the Scientific Advisory Committee on Nutrition (SACN). Hence, this process is currently on hold whilst the SACN/COT Joint Working Group on Plant Based Drinks considers plant-based drinks.

1.139 The COT agreed in July 2021 that Cow’s milk should act as the main comparator for plant-based drinks and therefore a statement on potential chemical risks from Cow’s milk was formulated.

1.140 Within this statement, the COT reviewed an extensive range of chemical compounds that could be present incidentally or as contaminants in cow’s milk to allow comparison with plant-based dairy alternatives. The COT concluded that the vast majority of potential contaminants assessed presented no risk of adverse health effects in children aged 6 months to 5 years of age at the levels observed within cow’s milk. The exceptions are iodine, BaP and PAH4, AFM1 specifically and total aflatoxins due to the contribution of AFM1, for which any risk to health in children aged 6 months to 5 years of age is unlikely but cannot be completely excluded. The possible risks to health in these age groups

from exposure to isoflavones in cow's milk is unknown, as no HBGVs have been established for these compounds in young children and hence there is a lack of knowledge on the toxicological significance of the levels that might be found in cow's milk.

1.141 The full statement can be found using this link: Background - Statement on the risk assessment of cow's milk in children aged 1 to 5 years, in the context of plant-based drinks evaluations | Committee on Toxicity (food.gov.uk)

1.142 A lay summary will be published in 2024.

Review of dioxins – draft systematic review

1.143 Following the Committee's assessment of the scientific basis and implications for risk management of the 2021 EFSA tolerable weekly intake (TWI) for dioxins and dioxin-like polychlorinated biphenyls (PCBs), the COT decided to undertake their own review of the relevant endpoints.

1.144 The Committee acknowledged that the review of dioxins would be an extensive and lengthy undertaking. To assist with the work, a systematic literature review on dioxins was commissioned, focusing on the relevant endpoints; male reproductive toxicity, immunotoxicity, the mechanism of action of dioxins via the aryl hydrocarbon receptor (AhR), and covering a predefined time frame from 2017 to 2021. The review also included a non-systematic consideration of the data on the potential carcinogenicity of dioxins and dioxin-like PCBs and whether this involved a genotoxic mechanism.

1.145 The Committee considered the commissioned report detailed and to provide a large amount of data for review. However, information from lower scoring studies was excluded from the report. As these studies could potentially hold relevant information to the overall assessments, the Committee agreed that there currently was not sufficient evidence to identify a key study or studies on which to establish a health-based guidance value (HBGV) and further consideration would be required.

1.146 Additional work in this area will commence in 2024.

Advice on the risk to human health from consumption of bivalve molluscs (shellfish) harvested from UK waters associated with marine biotoxins

1.147 The Food Standards Agency (FSA) is considering the current advice and monitoring programme for marine biotoxins and whether there is a need to update or change existing legislation in the UK. The main purpose of this work is to identify any emerging marine biotoxin threats in UK waters, including considerations on increasing occurrence with increasing temperatures due to climate change. The views of the COT were sought on whether any of these marine biotoxins would pose a risk to human health.

1.148 The FSA programme of work included a scoping paper on emerging marine biotoxins to be discussed by the Committee, the marine biotoxins reviewed were selected based on published assessments and reports on emerging marine biotoxins by other authorities, as well as a brief literature search. There was also specific consideration of pinnatoxin (PnTX) and pectenotoxin (PTX), due to the recent availability of additional analytical standards and the recent removal from the EU monitoring programme, respectively.

Scoping paper on the advice on the risk to human health from consumption of bivalve molluscs (shellfish) harvested from UK waters associated with marine biotoxins

1.149 The Committee considered the emerging marine biotoxins of potential concern to human health, i.e., brevetoxins, cyclic imines, palytoxins, saxitoxins, tetrodotoxins, novel azaspiracid analogues, novel paralytic shellfish poisoning (PSP) analogues and domoic acid analogues, and cyanobacteria toxins. There was a substantial amount of data available on the toxicology and occurrence on a number of the toxins, most of which are known and have the potential to be of concern to human health. However, the potential risk of these toxins depends on their occurrence, and this data, especially for UK waters and shellfish is lacking. The lack of occurrence data however did not exclude the possibility that these toxins were present in UK waters.

1.150 The Committee considered that to reach a conclusion on which of the marine biotoxins discussed would be of potential risk to UK consumers, further work is required, identifying, and tabulating the toxicological endpoints, lethal doses and occurrence data. It would be also useful to include information on the marine biotoxins which are already monitored and regulated, to put the potential risk of these emerging toxins into perspective.

1.151 The Committee will continue its work in 2024, aiming to identify the criteria to be fulfilled for a marine toxin to raise concern and consider how the previously discussed emerging marine biotoxins align with these criteria.

Pinnatoxin Group

1.152 Pinnatoxins (PnTXs) are a group of paralytic neurotoxins that can be found in filter-feeding bivalve shellfish such as scallops and mussels. Although no confirmed cases of PTX intoxication have been reported in humans, ingestion of PnTXs compounds by rodents under laboratory conditions can cause paralysis, respiratory depression, and death. PnTXs are not currently regulated in England or Wales, but with the availability of new analytical standards, future monitoring programs of PnTX could aim to include PnTX-G, -E and -F.

1.153 The COT was asked by the FSA to evaluate and consider the current toxicological evidence and the potential public health risk related to PnTXs. Considerations was also given to the likelihood of PnTXs becoming more prevalent due to climate change and rising sea water temperatures around the UK.

1.154 The Committee agreed that the toxicological data base for PnTx was limited. Although some acute toxicity studies existed in mice, there were substantial evidence gaps for both the toxicity of PnTX and the exposure in humans. Overall, the Committee concluded that due to the lack of toxicological and occurrence data on PnTX it was not possible to determine the extent of any public health risk relating to PnTXs. Although no human intoxications have been reported to date and there is no strong evidence to suggest PnTXs are a risk to humans, based on the limited data the Committee was unable to fully exclude a risk.

1.155 Members concluded that if the technology, i.e., chemical analysis, was already in place in the UK it would be reasonable to include PnTX in any monitoring programme.

Pectenotoxin group

1.156 PTXs are a group of toxins associated with diarrhetic shellfish poisoning (DSP) which are produced by dinoflagellate algae. They are accumulated by filter-feeding shellfish such as scallops and mussels. Although no confirmed cases of PTX intoxication have been reported in humans, ingestion of certain PTX compounds by rodents under laboratory conditions can cause gastrointestinal

symptoms and liver toxicity. PTXs are a regulated biotoxin group in the UK and are included in the group of toxins which are monitored routinely in UK shellfish.

1.157 The COT was asked by the FSA to consider the evidence in the 2009 EFSA opinion on pectenotoxin which was the basis for recent amendments to the European Union (EU) legislation removing PTXs from the list of monitored biotoxins in EU shellfish. In their 2009 opinion, EFSA concluded that PTXs were less toxic than okadaic acid (OA) - the toxin they are currently jointly regulated with– but when administered via the oral route, they have a different toxicological mode of action (MoA) and that they do not induce diarrhoea.

1.158 The COT found there was limited scientific data regarding the toxicity of PTXs, and the data that exist were for acute/short term exposure, rather than exposure over a prolonged period. Most of the available data were from rodent studies where PTX was administered via injection, which was not directly relevant to assessing the risk of intoxication by shellfish consumption in humans. Considering only the studies where PTX was orally administered to rodents, the Committee found the evidence was sufficient that PTX has a lower oral toxicity than OA. They also agree with EFSA that PTXs has a different MoA to OA and agreed that PTX should therefore not be expressed in OA equivalents. However, the Committee considered the evidence that PTX-group toxins do not cause diarrhoea inconclusive, with some studies in rodents reporting diarrhoea after PTX administration.

1.159 Overall, the Committee concluded that based on effects seen in animals a toxicological risk from exposure to PTX was plausible, albeit probably low. However due to the lack of toxicological and occurrence data on PTX it was currently not possible to determine the extent of any public health risk of PTXs.

Assessment and draft interim position statement on bisphenol A (BPA)

1.160 Following public consultation in 2022, the EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) established a new tolerable daily intake (TDI) of 0.2 ng Bisphenol A (BPA)/kg bw per day in April 2023.

1.161 The Committee discussed the final opinion published by EFSA and confirmed that they did not support EFSA’s conclusion that the observed change in the number Th17 white blood cells would continuously result in an adverse immune effect/inflammatory response. hrs was an intermediate endpoint and was not appropriate to derive a point of departure (POD) and subsequently a TDI.

Given the uncertainties over the endpoint a more robust and transparent weight of evidence (WoE) approach and evidence integration should have been applied to a wider dataset to derive a more reliable and relevant endpoint on which to base a health-based guidance value (HBGV).

1.162 Following their diverging view from EFSA, the Bundesinstitut fuer Risikobewertung (BfR) published a full assessment of BPA in 2023, deriving a TDI of 0.2 µg/kg bw per day (equivalent to 200 ng/kg bw per day) based on (male) reproductive effects.

1.163 While assessments of BPA by other authorities pre-dated the EFSA 2023 assessment, and were therefore not considered relevant, the Committee considered the BfR approach in more detail and concluded that the endpoint applied and approach taken was reasonable, albeit with a significant level of conservatism, and was in line with previous approaches taken by the Committee themselves.

1.164 Overall, the Committee considered it possible that the current UK TDI for BPA would need to be revised to account for new evidence and ensure it was sufficiently protective. However, on balance the weight of evidence did not support the conclusions drawn by EFSA, or a TDI set as low as that derived by EFSA. The Committee instead agreed that the BfR approach was reasonable and to apply the TDI of 0.2 µg/kg bw per day as an interim measure.

1.165 The Committee will undertake their own weight of evidence approach and assessment of BPA in due course.

1.166 The work on BPA is ongoing but an interim position statement highlighting the discussions and considerations of the Committee will be published in spring 2024.

Aircraft cabin air

1.167 In 2007, the COT published a statement on aircraft cabin air, having been asked by the Department for Transport (DfT) to undertake an independent scientific review of data submitted by the British Airline Pilots Association (BALPA) relating to organophosphate (OP) compounds, the cabin air environment, ill-health in aircraft crews and the possible relationship to smoke/fume events in aircraft, due to concerns about the possible effects on aircrew health of oil/hydraulic fluid smoke/fume contamination incidents in commercial aircraft (COT, 2007).

1.168 In 2013, DfT asked the COT to undertake an independent scientific review of the results of DfT-funded aircraft cabin environment research commissioned in response to recommendations made by COT in 2007, after which the COT issued a position statement on cabin air (COT, 2013).

1.169 The COT was recently asked by DfT to investigate whether any new data have been published and to re-evaluate their previous views, and in particular consider the question “Is there evidence of exposure to chemical contaminants in cabin air that could have long-term health impacts, either from acute exposures or due to long-term low level exposures including mixtures, e.g., of volatile organic compounds (VOCs)?”.

1.170 In 2023, the Committee continued this consideration and reviewed discussion papers on concentrations of VOCs in European aircraft and comparison with regulatory standards and health-based guidelines and a paper on the basis of the regulatory values for carbon dioxide. The COT also considered drafts of the statement on this topic, and it is anticipated that the statement will be finalised in 2024.

Sub-statement on the potential risk(s) from exposure to microplastics: Inhalation route

1.171 In 2019, as part of horizon scanning, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) identified the potential risks from microplastics as a topic it should consider to inform Food Standards Agency (FSA) discussions on this (TOX/2019/08). Since then, several discussion papers have been presented to the COT and in 2021, the COT published an overarching statement on the potential risks from exposure to microplastics (COT Statement 2021/02). This document provided a high-level overview of the current state of knowledge, data gaps and research requirements with regards to this topic.

1.172 There is evidence for the presence of plastic particles in the air (indoor and outdoor) and thus inhalation is a possible route of exposure.

1.173 The purpose of the sub-statement was to provide supplementary material to the overarching statement on microplastics (COT Statement 2021/02) and to consider in detail the potential toxicological risks of exposure from microplastics via the inhalation route (i.e., exposure resulting from the presence of microplastics in the air (indoor, outdoor and occupational settings)). It is based on currently available literature and data from internal tools at the UK FSA (these

internal tools include: a literature search application and signal prioritising dashboards).

1.174 The final draft of this paper was presented at the end of 2023 and will be published in 2024, completing the current work on microplastics.

Novel formulations of supplement compounds designed to increase oral bioavailability

1.175 In the discussions on the safety of turmeric in 2022 the COT identified novel formulations, particularly those with the potential to increase oral bioavailability, as a key area of uncertainty in the risk assessment of dietary supplements. Such formulations include micellar, nano- and micro-formulations, including colloidal dispersions and liposomal systems. Therefore, the Committee proposed that novel formulations designed to increase the oral bioavailability of supplements should form the basis of a general discussion paper.

1.176 The Committee considered an overview of the structure and physicochemical properties of several novel supplement formulation types, including colloidal, liposomal, and micellar systems. The biological mechanisms through which such formulations may alter bioavailability were also reviewed. Pharmacokinetic studies in human subjects with novel formulations of three different supplements were reviewed as exemplars: vitamin C, curcumin, and cannabidiol (CBD).

1.177 In terms of establishing health-based guidance values (HBGVs) for novel supplement formulations, it was noted that this was important for consumer safety, as maximum dosage levels for certain compounds may not be applicable to novel formulations of the same compounds. The Committee concluded that the critical factor was understanding how external dose related to internal exposure for standard and novel formulations, and when/if these diverged. In the absence of specific kinetic data, it was stated that a worst-case approach would be to assume 100% bioavailability of the active compound. The Committee noted that these data are often unavailable, and that the pharmaceutical industry is likely to have more extensive datasets that might aid in these kinds of assessments.

1.178 The Committee agreed that they had reviewed sufficient information to reach general conclusions regarding novel formulations, and that no further and/or specific information was required. The Committee also agreed, given that supplements would vary on a case-by-case basis, it was not necessary to provide further case studies and/or exposure assessments to reach general conclusions.

1.179 As a next step, a position paper will be drafted in 2024 that summarises the Committees comments, which could potentially be included in future guidance documents.

UK COT FSA New Approach Methodologies Roadmap (2023) Draft Version 3

1.180 The UK FSA and the COT have been considering New Approach Methodologies (NAMs) to understand the best scientific methodologies available for use in the risk assessment of chemicals and to consider how these can be incorporated and accepted in a regulatory context.

1.181 In order to achieve this, the FSA and COT are developing a UK New Approach Methodologies (NAMs) roadmap towards acceptance and integration of NAMs including predictive toxicology methods using computer modelling into safety and risk assessments for regulatory decision making. This will not only require the historic 3Rs approach (replacement, reduction and refinement of animal experiments) but the expansion to the 6R principle which also includes reproducibility, relevance, and regulatory acceptance.

1.182 Following presentation of the roadmap at various international conferences, meetings and workshops, Members were asked to note and comment on the recent updated draft version of UK NAMs roadmap which incorporates the feedback received. This includes data integrity and capability, training and the integrated transition into acceptance.

1.183 Work on the roadmap will continue including incorporating any additional information gathered from conferences, meetings, and workshops as well as the outputs from the FSA literature review on New Approach Methodologies (NAMs) to Support Regulatory Decisions for Chemical Safety.

Draft joint statement on the request for an assessment of tetra-methyl bisphenol F diglycidyl ether (TMBPF-DGE) in canned food packaging materials

1.184 The Committee discussed the draft assessment on tetra-methyl bisphenol F diglycidyl ether (TMBPF-DGE), following previous discussions by the COT, the Joint Expert Group on Food Contact Materials (FCM JEG) and sister Committee on Mutagenicity (COM). The work is ongoing, but publication of the final assessment is expected in spring 2024. This item is reserved as the data are

commercially confidential.

Assessment of ocean bound plastic (OBP)

1.185 The Food Standards Agency (FSA) and Food Standards Scottland (FSS) are currently undertaking work on the potential use of plastic materials from the open environment in food packaging applications, specifically plastic materials intercepted before entering the marine environment.

1.186 Following initial discussions by the Joint Expert Group on Food Contact Materials (FCM JEG) and COT, the FSA and FSS undertook a call for evidence between March and October 2022, this was followed by additional data collection from the companies that engaged with the call, upon enquiry by the FCM JEG. Additional companies were also identified as suppliers of these materials between November 2022 and January 2024, and were contacted for any information they may hold.

1.187 The FCM JEG has assessed all information provided to the FSA and FSS to date and is currently in the process of drafting the final assessment, publication is expected in spring 2024.